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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/034,692	12/27/2001	Peter Gill	7500.331USC1	2411

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EXAMINER	
STRZELECKA, TERESA E	
ART UNIT	**PAPER NUMBER**
1637	

DATE MAILED: 03/09/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

HL

Office Action Summary	Application No.	Applicant(s)	
	10/034,692	GILL ET AL.	
	Examiner	Art Unit	
	Teresa E Strzelecka	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 December 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *2,4,5,8,9,18-20,26-45 and 47-63* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *2,4,5,8,9,18-20,26-45 and 47-63* is/are rejected.

7)☒ Claim(s) *2,4,5,8,9,18-20,26-45 and 47-63* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *12/27/2001*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. This application has been transferred to Examiner Teresa Strzelecka in the Art Unit 1637, since Examiner Spiegler left the USPTO.

2. This office action is in response to an amendment filed December 29, 2004. Claims 1-46 were previously pending, with claim 46 withdrawn from consideration. Applicants cancelled claims 1, 3, 6, 7, 10-17, 21-25 and 46, amended claims 2, 4, 5, 8, 9, 18-20, 26-28, 30-36, 38-42 and 45, and added new claims 47-63. Claims 2, 4, 5, 8, 9, 18-20, 26-45 and 47-63 are pending and will be examined.

3. Applicants' amendments and claim cancellations overcame the following: rejection of claims 1-45 under 35 U.S.C. 112, second paragraph; rejection of claims 1-16 and 21-45 under 35 U.S.C. 102(b) as anticipated by Paranavitana; rejection of claims 17-20 under 35 U.S.C. 103(a) over Paranavitana and Wu et al. and objection to claim 18.

4. Applicants' amendments to the specification obviated the following objections: objection with respect to the abstract; objection to the Brief Description of Drawings; objection to Fig. 7 not containing SEQ ID NO. Applicants' arguments obviated the objection to Figures 11, 21 and 25.

5. Applicants' arguments regarding art rejections are moot in view of the new rejections presented in this office action.

6. The IDS filed December 27, 2001, in which the first three references were not considered, has been considered.

Claim Objections

7. Claims 47, 2, 4, 5, 8, 9, 18-20, 26-45 and 48-63 are objected to because of the following informalities: "complimentary" instead of "complementary" in line 18 of claim 47. Appropriate correction is required.

Claim Rejections - 35 USC § 112

8. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

9. Claims 2, 4, 5, 8, 9, 18-20, 26-45 and 47-63 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A) Claims 2, 4, 5, 8, 9, 18-20, 26-45 and 47-63 are indefinite in claim 47. Claim 47 is indefite over the recitation of "the first sets of primers" in line 3. In the same line there is a limitation "a first set of primers". Therefore, it is not clear whether Applicants intended a limitation of a single set of first primers or multiple sets of first primers.

B) Claims 37-40 are indefinite, since they depend from cancelled claim 1.

C) Claim 43 recites the limitation " each probe " in line 1. There is insufficient antecedent basis for this limitation in the claim. Neither claim 41 nor claim 47, from which claim 43 depends, include a limitation of a probe.

D) Claim 43 is indefinite over the recitation of "one or more probes having sequences which at least in part are different from one another". It is not clear how one probe can have different sequences which are different from each other.

E) Claim 44 recites the limitation " the probes " in line 1. There is insufficient antecedent basis for this limitation in the claim. Neither claim 41 nor claim 47, from which claim 44 depends, include a limitation of a probe or probes.

F) Claim 45 recites the limitation " the probes " in lines 1 and 2. There is insufficient antecedent basis for this limitation in the claim. Neither claim 41 nor claim 47, from which claim 45 depends, include a limitation of a probe.

G) Claim 52 recites the limitation " the first sets of primers " in line 1. There is insufficient antecedent basis for this limitation in the claim. Claim 47, from which claim 52 depends, recites the limitation of a "first set of primers".

H) Claim 54 recites the limitation " the forward primers " in line 1. There is insufficient antecedent basis for this limitation in the claim. Claim 47, from which claim 54 depends, does not contain a limitation of a forward primer.

I) Claim 55 recites the limitation " the forward primers " in lines 2 and 5. There is insufficient antecedent basis for this limitation in the claim. Neither claim 63 nor claim 47, from which claim 55 depends, contain a limitation of a forward primer.

J) Claim 59 recites the limitation " the second further portion " in line 1. There is insufficient antecedent basis for this limitation in the claim. Claim 47, from which claim 59 depends, does not contain a limitation of a second further portion.

Claim Interpretation

10. The terms "first set of primers" and "second set of primers" have not been defined by Applicants. Therefore, the term "a set of primers" is interpreted as two or more primers, which may or may not have the same sequence.

11. Applicants have not defined the term "characteristic", therefore it is interpreted as any feature of the amplified product.

12. Applicants have not defined the term "distinctive unit", therefore it is interpreted as any entity which is introduced by hybridization of a sequence complementary to the further portion of the amplified product.

13. Applicants have not defined the term "side of the SNP", therefore it is interpreted as any sequence comprising the SNP.

14. Applicants have not defined the term "attachment unit", therefore it is interpreted as any part of the amplified product.

15. Applicants have not defined the term "the base before the base which is the SNP", therefore, any base in the vicinity of the SNP is considered to be "before the SNP".

Claim Rejections - 35 USC § 102

16. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

17. Claims 47, 2, 4, 5, 8, 9, 18-20, 26, 27, 32-45 and 48-63 are rejected under 35 U.S.C. 102(b) as being anticipated by Whitcombe et al. (GB 2 312 747 A; cited in the IDS).

Regarding claim 47, Whitcombe et al. teach detection of single nucleotide polymorphisms in a sample containing DNA (page 5, lines 24-30), the method comprising:

contacting DNA from the DNA containing sample with a first set of primers, the first sets of primers including two or more primers, a primer having a locus specific portion and a further portion, the further portion of at least one of the primers being different from the further portion of at least one of the other primers (Whitcombe et al. teach contacting a DNA sample (page 9, lines 27-30; page 10, line 1) with a first set of primers, where the primers have a genome-specific (= locus specific) portion and a tail portion (= further portion). The tail region comprises a tag portion and a detector portion (Fig. 9a; page 1, lines 20, 21; page 4, lines 22-25). The tail sequences on the primers may be different (page 4, lines 8, 9), therefore, Whitcombe et al. anticipate the limitation of the further portion of one of the primers being different from the further portion of at least one other primer).)

amplifying the DNA, the amplification using the first set of primers to give an amplified product, the amplified product including a sequence complementary to the locus specific portion and further portion of a first set primer (Whitcombe et al. teach amplification of the DNA using diagnostic primers (= the first set of primers) to give an amplified product including a sequence complementary to the locus specific portion and further portion (page 1, lines 28-31; page 2, lines 1-7; Fig. 9(b); Fig. 13 (a).),

contacting at least a portion of the amplified product with at least one second set of primers (Whitcombe et al. teach contacting the amplified product with tag primers (= second set of primers) (page 2, lines 7-10; page 4, lines 22-25).),

amplifying the first amplified product to give a further amplified product by annealing at least one of the second set of primers to that part of the first amplified product with a sequence complementary to the further portion (Whitcombe et al. teach contacting the amplified product with tag primers (= second set of primers) which are complementary to the complement of a tag portion (page 2, lines 7-10; page 3, lines 17-25; Fig. 10(b)), producing an amplification product (= further amplified product).) and;

examining one or more characteristics of the further amplified product using the presence or absence of a distinctive unit introduced by hybridisation or annealing of a component to the sequence complementary to the further portion, the component including the distinctive unit, the one or more characteristics providing information on the single nucleotide polymorphisms in the DNA containing sample (Whitcombe et al. teach analyzing the amplified product by detecting the detector region of the amplified product, where the presence or absence of the detected sequence is determined using a detectable signal. The detector region may be detected using a labeled hybridization probe (where label = distinctive unit) (page 2, lines 11-31).).

Regarding claims 2, 54 and 63, Whitcombe et al. teach primers with SNP identifying portions, where the portions are different for each primer, and where the primers anneal to one side of the SNP (page 5, lines 24-30; page 20, lines 10-15; page 21, lines 3-8 and 27-31; page 22, line 1 and 20-26).

Regarding claim 4, Whitcombe et al. teach primers which pair with locus sequence (page 4, lines 22, 23) at the vicinity of the SNP (page 5, lines 24-30).

Regarding claims 5 and 8, Whitcombe et al. teach primers with SNP identifying portions for each possible SNP under investigation and a reverse primer (page 5, lines 24-30; page 20, lines 10-15; page 21, lines 3-8 and 27-31; page 22, line 1 and 20-26).

Regarding claim 9, Whitcombe et al. teach primers which have a tail portion (= further portion) which is not complementary to the locus sequence (page 3, lines 26, 27; Fig. 9a).

Regarding claim 18, Whitcombe et al. teach fluorescently labeled probes (page 2, lines 30, 31; page 11, lines 25-30; page 12, lines 1-12; Fig. 10) and molecular beacons (page 12, lines 13-28; Fig. 11).

Regarding claim 19, Whitcombe et al. teach a second set of primers with a 5' end, where the primers have different labels (= distinctive units) (page 10, lines 5-9).

Regarding claim 20, Whitcombe et al. teach detection of the detector region as being indicative of the presence or absence of the single base being detected (page 2, lines 2-5 and 11-15).

Regarding claim 26, Whitcombe et al. teach concentration of the second set of primers relative to the concentration of the first set of primers of at least 20:1, 30:1, 40:1 or 50:1 (page 9, lines 20-24), therefore anticipating the limitation of the ratio being at least 5:1.

Regarding claim 27, Whitcombe et al. teach the diagnostic and tag primers present in the same reaction, concentration of the first set of primers of 10 nM and concentration of the second set

of 500 nM (page 20, lines 20-28), therefore anticipating the ranges of between 10 and 200 nM for the first primers and 400 to 4000 nM for the second primers.

Regarding claim 32, Whitcombe et al. teach the annealing temperature being 62 C for 42 cycles (page 21, line 1).

Regarding claim 33, Whitcombe et al. teach amplification using two or more sets of first primers and one set of second primers and separation of the amplification products by gel electrophoresis (page 18, lines 17-24; page 19, lines 6-8).

Regarding claim 34, Whitcombe et al. teach contacting the amplified product with a capture probe (= retained component) on solid support, which hybridizes to the detector region of the amplified product (page 2, line 31; page 3, lines 1-3; Fig. 13).

Regarding claim 35, Whitcombe et al. teach annealing of the probe to the tail region of the amplified product (Fig. 13), therefore, they inherently teach hybridization of the probe up to a base before the base which is the SNP.

Regarding claim 36, Whitcombe et al. annealing of the probe to the tail region of the amplified product (page 2, line 31; page 3, lines 1-3; Fig. 13).

Regarding claim 41, Whitcombe et al. teach the detector region being complementary to a capture probe which may be used to immobilize the amplification product (page 2, line 31; page 3, lines 1-3). Therefore, the detector region is an attachment unit.

Regarding claims 42 and 43, Whitcombe et al. teach detecting the attached amplified product with probes different from the capture probe which have a common sequence portion corresponding to the locus specific portion of the amplified product (Fig. 13(b); page 14, lines 10-15).

Regarding claims 44 and 45, Whitcombe et al. teach probes with different sequence portions complementary to the tail region of the amplified products, where the distinctive units are the different sequences of the probes (page 16, lines 10-20; Fig. 17).

Regarding claims 48 and 59, Whitcombe et al. teach the tag primers (= second primers) having a sequence (= second further portion) which matches the sequence of the tag portion (= further portion) of the first set of primers (page 1, lines 20-31; page 2, lines 1-10; page 3, lines 17-21).

Regarding claim 49, Whitcombe et al. teach introduction of a label during the amplification process using labeled dNTPs (page 3, lines 5, 6).

Regarding claim 50, Whitcombe et al. teach introduction of a label on a probe which hybridizes to the amplification product, therefore, subsequently to the amplification process (page 2, lines 27-31).

Regarding claim 51, Whitcombe et al. teach detection of the amplification product with a probe (= component) complementary to the detector region of the amplified product (page 2, lines 27-31).

Regarding claim 52, Whitcombe et al. teach a first set of primers consists of two forward primers and one reverse primer (page 20, lines 10-15; page 21, lines 3-8 and 27-31; page 22, line 1 and 20-26).

Regarding claim 53, Whitcombe et al. teach the tail portion of the first set of primers attached to the 5' end of the locus specific portion (Fig. 9(a)).

Regarding claims 55 and 56, Whitcombe et al. teach a set of primers in which a terminal nucleotide of one of the primers is complementary to a normal nucleotide and another primer is complementary to a variant nucleotide (page 5, lines 24-31), therefore, they teach one primer

annealing to the 3' side of the normal SNP, for example, because it matches the normal nucleotide, and the other primer does not anneal to the 3' side of the normal SNP, since it does not match the normal SNP.

Regarding claim 57, Whitcombe et al. teach one set of second primers (page 20, lines 10-15; page 21, lines 3-8 and 27-31; page 22, line 1 and 20-26).

Regarding claim 58, Whitcombe et al. teach primer sets with two forward primers and a reverse primer (page 20, lines 10-15; page 21, lines 3-8 and 27-31; page 22, line 1 and 20-26).

Regarding claim 60, Whitcombe et al. teach a plurality of first sets of primers and resulting amplification products having different lengths (page 7, lines 6-15 and 25-31).

Regarding claims 61 and 62, Whitcombe et al. teach providing two sets of amplifying conditions, one for amplification with the diagnostic primers and one for amplification using the tag primers, where the first set amplification conditions favors amplification of the diagnostic primers but not the tag primers (page 5, lines 6-10).

Claim Rejections - 35 USC § 103

18. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

19. Claims 28-31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Whitcombe et al. (GB 2 312 747 A; cited in the IDS).

A) Regarding claims 28-31, Whitcombe et al. teach the diagnostic and tag primers present in the same reaction (page 20, lines 20-28) and the tag primers having a melting temperature higher than the melting temperature of the diagnostic primers (page 5, lines 6-10). They teach different

annealing temperatures for cycles 1-2, which favor priming with the first primers and 3-40, which favor priming with tag primers (page 20, lines 30, 31; page 32, lines 1 and 23-25; page 22, lines 15-19; page 23, lines 10-13), where the annealing temperatures vary depending on the sequences and lengths of the primers.

Therefore, claims 28-31 are drawn to optimizing the cycling conditions. It would have been *prima facie* obvious to perform routine optimization using reagents, as noted in *In re Aller*, 105 USPQ 233 at 235,

> More particularly, where the general conditions of a claim are disclosed in the prior art, it is not inventive to discover the optimum or workable ranges by routine experimentation.

Routine optimization is not considered inventive and no evidence has been presented that the selection of specific annealing temperatures or number of cycles was other than routine, that the products resulting from the optimization have any unexpected properties, or that the results should be considered unexpected in any way as compared to the closest prior art.

20. No claims are allowed.

Conclusion

21. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be

calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Teresa E Strzelecka whose telephone number is (571) 272-0789. The examiner can normally be reached on M-F (8:30-5:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571) 272-0782. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

TS
March 3, 2005

JEFFREY FREDMAN
PRIMARY EXAMINER
3/7/05